

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application:

1. (Currently amended) A method of identifying and selecting therapeutic compounds having a predetermined core structure, said method comprising:

establishing a relationship between physical-chemical profile and biological activity; wherein the physical-chemical profile comprises one or more parameters selected from ~~onset of oxidation, potential of oxidation, potential of reduction,~~ reversibility of one or more oxidation waves [[,]] or reversibility of one or more reduction waves [[,]] ~~current of oxidation or current of reduction~~; and wherein the biological activity is measured in an assay effective in detecting compounds for the treatment of a targeted disorder;

testing further potential therapeutic candidates with said core structure for their physical-chemical properties; and

selecting therapeutic compounds based on their physical-chemical parameters falling within a range predefined by the physical-chemical/biological relationship of the previously tested subset of compounds.

2. (Cancelled)

3. (Cancelled)

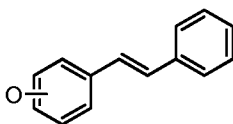
4. (Cancelled)

5. (Original) The method of claim 1, wherein the physical-chemical profile comprises the parameter for reversibility of one or more oxidation waves.

6. (Original) The method of claim 1, wherein the physical-chemical profile comprises the parameter for reversibility of one or more reduction waves.
7. (Cancelled)
8. (Cancelled)
9. (Withdrawn) A therapeutic composition for treating a condition characterized by oxidative stress comprising a compound selected according to the method of claim 1 and a therapeutically acceptable excipient.
10. (Currently amended) The method of claim 1, wherein the ~~biological~~ assay is a cell-based assay comprising one or more assays selected from the High Glutamate-Induced Oxidative Stress (HGOS) assay wherein the compounds in the previously tested subset group of compounds have the ability to protect at least 30% of energetically competent cells against stressor induced cell death; and the E-selectin (ELAM) assay wherein the compounds in the previously tested subset group of compounds exhibit an EC₅₀ lower than about 30 μ M.
11. (Original) The method of claim 10, wherein the therapeutic compound is selected if it comprises a stilbene core structure and if its physical-chemical profile comprises one or more parameters selected from the parameter for potential of the first oxidation wave that falls between about 800 mV and 1400 mV versus a silver/silver chloride reference electrode, and the parameter for the reversibility of the first oxidation wave that measures about 20% or more.
12. (Original) The method of claim 11, wherein the physical-chemical profile additionally comprises one or more parameters selected from the energy profile parameters and the transport profile parameters.

13. (Original) The method of claim 11, wherein the therapeutic compound is for the treatment of a condition characterized by oxidative stress.
14. (Original) The method of claim 10, wherein the therapeutic compound is selected if it comprises a core structure of Formula I:

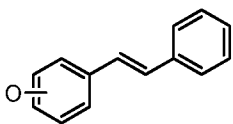
Formula I



wherein additional substitution at the phenyl rings does not include a nitro group; and if its physical-chemical profile comprises the parameter for potential of the first oxidation wave that falls below 1000 mV versus a silver/silver chloride reference electrode.

15. (Original) The method of claim 14, wherein the physical-chemical profile additionally comprises one or more parameters selected from the energy profile parameters and the transport profile parameters.
16. (Original) The method of claim 14, wherein the therapeutic compound is for the treatment of a condition characterized by oxidative stress.
17. (Original) The method of claim 10, wherein the therapeutic compound is selected if it comprises a core structure of Formula I:

Formula I



wherein additional substitution at the phenyl rings includes a nitro group; and if its physical-chemical profile comprises one or more parameters selected from the parameter for potential of the first oxidation wave that falls between about 950 mV and 1250 mV versus a silver/silver chloride reference electrode, and the parameter for reversibility of the first oxidation wave measures more than 20%.

18. (Original) The method of claim 17, wherein the physical-chemical profile additionally comprises one or more parameters selected from the energy profile parameters and the transport profile parameters.
19. (Original) The method of claim 17, wherein the therapeutic compound is for the treatment of a condition characterized by oxidative stress.
20. (Withdrawn) A therapeutic composition for treating a condition characterized by oxidative stress comprising a compound selected according to the method of claim 11 and a therapeutically acceptable excipient.
21. (Withdrawn) The composition of claim 20, wherein the condition is inflammation, neurodegeneration or ischemia.
22. (Withdrawn) A therapeutic composition for treating a condition characterized by oxidative stress comprising a compound selected according to the method of claim 14 and a therapeutically acceptable excipient.
23. (Withdrawn) The composition of claim 22, wherein the condition is inflammation, neurodegeneration or ischemia.
24. (Withdrawn) A therapeutic composition for treating a condition characterized by oxidative stress comprising a compound selected according to the method of claim 17 and a

therapeutically acceptable excipient.

25. (Withdrawn) The composition of claim 24, wherein the condition is inflammation, neurodegeneration or ischemia.

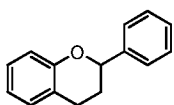
26. (Currently amended) ~~The method of claim 3,~~ A method of identifying and selecting therapeutic compounds having a predetermined core structure, said method comprising:

establishing a relationship between physical-chemical profile and biological activity; wherein the physical-chemical profile comprises the a parameter for onset of oxidation; and wherein the biological activity is measured in an assay comprising and the biological assay comprises the E-selectin (ELAM) cell based assay detecting compounds with an EC₅₀ lower than 30 μ M;

testing further potential therapeutic candidates with said core structure for their physical-chemical properties; and

selecting therapeutic compounds based on their physical-chemical parameters falling within a range predefined by the physical-chemical/biological relationship of the previously tested subset of compounds.

27. (Original) The method of claim 26, wherein the therapeutic compound is selected if it comprises a flavonoid core structure of Formula II:

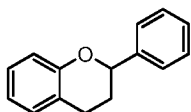


Formula II

wherein none of the substituents are hydroxy groups;

and if its physical-chemical profile comprises the parameter for onset of oxidation that falls between about 850 mV and 1050 mV versus a silver/silver chloride reference electrode.

28. (Original) The method of claim 27, wherein the physical-chemical profile additionally comprises one or more parameters selected from the energy profile parameters and the transport profile parameters.
29. (Original) The method of claim 27, wherein the therapeutic compound is for the treatment of a condition characterized by inflammation.
30. (Original) The method of claim 26, wherein the therapeutic compound is selected if it comprises a flavonoid core structure of Formula II:



Formula II

- wherein one or more of the substituents are hydroxy groups;
- and if its physical-chemical profile comprises the parameter for onset of oxidation that falls between about 350 mV and 650 mV versus a silver/silver chloride reference electrode.
31. (Original) The method of claim 30, wherein the physical-chemical profile additionally comprises one or more parameters selected from the energy profile parameters and the transport profile parameters.
32. (Original) The method of claim 30, wherein the therapeutic compound is for the treatment of a condition characterized by inflammation.
33. (Currently amended) ~~The method of claim 4,~~ A method of identifying and selecting therapeutic compounds having a predetermined core structure, said method comprising:

establishing a relationship between physical-chemical profile and biological activity;

wherein the physical-chemical profile comprises ~~the~~ a parameter for potential of oxidation wave; and wherein the biological activity is measured in ~~and the cell-based~~ an assay ~~comprising~~ ~~comprises the~~ an HGOS assay protecting at least 30% of the cells against stressor induced cell death;

testing further potential therapeutic candidates with said core structure for their physical-chemical properties; and

selecting therapeutic compounds based on their physical-chemical parameters falling within a range predefined by the physical-chemical/biological relationship of the previously tested subset of compounds.

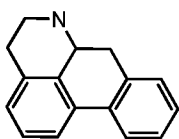
34. (Original) The method of claim 33, wherein the therapeutic compound is selected if it comprises a flavonoid core structure and if its physical-chemical profile comprises the parameter for oxidation potential that falls between about 1050 mV and 1450 mV versus a silver/silver chloride reference electrode.
35. (Original) The method of claim 34, wherein the physical-chemical profile additionally comprises one or more parameters selected from the energy profile parameters and the transport profile parameters.
36. (Original) The method of claim 34, wherein the therapeutic compound is for the treatment of a condition characterized by oxidative stress.
37. (Withdrawn) A therapeutic composition for treating a condition characterized by inflammation comprising a compound selected according to the method of claim 27 and a therapeutically acceptable excipient.

38. (Withdrawn) A therapeutic composition for treating a condition characterized by inflammation comprising a compound selected according to the method of claim 30 and a therapeutically acceptable excipient.
39. (Withdrawn) A therapeutic composition for treating a condition characterized by oxidative stress comprising a compound selected according to the method of claim 34 and a therapeutically acceptable excipient.
40. (Withdrawn) The composition of claim 39, wherein the condition is ischemia or neurodegeneration.
41. (Currently amended) ~~The method of claim 4,~~ A method of identifying and selecting therapeutic compounds having a predetermined core structure, said method comprising:

establishing a relationship between physical-chemical profile and biological activity; wherein the physical-chemical profile comprises ~~the~~ a parameter for potential of the first oxidation wave; and wherein the biological activity is measured in a ~~and the biological activity assay is the~~ Thioflavin T binding assay measuring reduction of amyloid- β fibril formation;

testing further potential therapeutic candidates with said core structure for their physical-chemical properties; and

selecting therapeutic compounds based on their physical-chemical parameters falling within a range predefined by the physical-chemical/biological relationship of the previously tested subset of compounds.
42. (Original) The method of claim 41, wherein the compound is selected if it comprises an apomorphine core structure of Formula III:

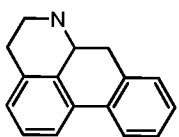


Formula III

and if the physical-chemical profile comprises the parameter for potential of the first oxidation wave that falls under 1250 mV versus a silver/silver chloride reference electrode.

43. (Original) The method of claim 42, wherein the physical-chemical profile additionally comprises one or more parameters selected from the energy profile parameters and the transport profile parameters.

44. (Original) The method of claim 41, wherein the compound is selected if it comprises an apomorphine core structure of Formula III:



Formula III

and if the physical-chemical profile comprises the parameter for potential of the first reduction is more negative than about -790 mV versus a silver/silver chloride reference electrode.

45. (Original) The method of claim 44, wherein the physical-chemical profile additionally comprises one or more parameters selected from the energy profile parameters and the transport profile parameters.

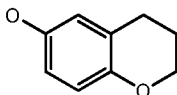
46. (Withdrawn) A therapeutic composition for treating a condition characterized by amyloid- β fibril formation comprising a compound selected according to the method of claim 42 and a therapeutically acceptable excipient.

47. (Withdrawn) The composition of claim 46, wherein the condition is Alzheimer's disease.
48. (Withdrawn) A therapeutic composition for treating a condition characterized by amyloid- β fibril formation comprising a compound selected according to the method of claim 44 and a therapeutically acceptable excipient.
49. (Withdrawn) The composition of claim 48, wherein the condition is Alzheimer's disease.
50. (Currently amended) The method of claim 6, wherein ~~the physical-chemical profile comprises the parameter for reversibility of reduction wave and~~ the biological activity assay comprises the E-selectin (ELAM) cell based assay detecting compounds with an EC₅₀ lower than 30 μ M versus a silver/silver chloride reference electrode.
51. (Previously presented) The method of claim 50, wherein the therapeutic compound is selected if it comprises a quinone core structure and if its physical-chemical profile comprises a parameter for the total reversibility of reduction of 75% or more.
52. (Original) The method of claim 51, wherein the physical-chemical profile additionally comprises one or more parameters selected from the energy profile parameters and the transport profile parameters.
53. (Original) The method of claim 51 wherein the compound is for the treatment of a condition characterized by oxidative stress.
54. (Withdrawn) A therapeutic composition for treating a condition characterized by oxidative stress comprising a compound selected according to the method of claim 51 and a therapeutically acceptable excipient.

55. (Withdrawn) The composition of claim 54, wherein the condition is inflammation, neurodegeneration, or ischemia.

56. (Original) The method of claim 33, wherein the therapeutic compound is selected if it comprises a chroman core structure of Formula IV,

Formula IV



and if its physical-chemical profile comprises the parameter for oxidation potential that falls between about 850 mV and 1200 mV versus a silver/silver chloride reference electrode.

57. (Original) The method of claim 56, wherein the physical-chemical profile additionally comprises one or more parameters selected from the energy profile parameters and the transport profile parameters.

58. (Withdrawn) A therapeutic composition for treating a condition characterized by oxidative stress comprising a compound selected according to the method of claim 57 and a therapeutically acceptable excipient.